

SHORTENED COAGULATION PROFILE IN PREGNANCY -COMPARATIVE ANALYSIS IN DIFFERENT TRIMESTERS - RETROSPECTIVE STUDY FROM A TERTIARY CARE CENTRE**Dr. Sarika Singh^{1*}, Dr. Bhavika Rishi² and Dr. Sunita Sharma²**Associate Professor Pathology Maulana Azad Medical College New Delhi.
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ABSTRACT

Introduction / Background: A state of hypercoagulation and low grade disseminated intravascular coagulation exists during the entire period of pregnancy and immediate postpartum period. While this is beneficial for preventing maternal hemorrhage during pregnancy and delivery, at the same time also predisposes the women for multiple complications (e.g. miscarriages, preeclampsia, intra-uterine growth restriction, etc.). Shortened aPTT (Activated partial thromboplastin time) is a marker of hypercoagulability observed in pregnancy and has been associated with increased incidence of venous thromboembolism (VTE). **Materials and methods:** This retrospective study was conducted at the Department of Pathology of a tertiary care hospital in North India, including pregnant women who were followed up in the antenatal clinic of the hospital. Objective of the study was to assess the prevalence of shortened Prothrombin time (PT) and aPTT in pregnant women and to further assess the incidence of pre mature rupture of membrane (PROM) and preeclampsia in those with an isolated shortened aPTT, during 3rd trimester and labor. Women with past history of thrombosis, antenatal hemorrhage and bad obstetric history were excluded. **Results:** Among 173 pregnant women included in the study 71.7% were detected to have a shortened PT, aPTT or both; the commonest abnormality was an isolated shortened aPTT (65/124). Most (83%) of the patients were in their 3rd trimester of pregnancy during which the highest prevalence of shortened aPTT (86%) was seen. Women with a shortened aPTT during 3rd trimester and labor were detected to have a very high incidence of PROM and preeclampsia. **Conclusion:** There is a high prevalence of shortened PT and aPTT in pregnant women and a shortened aPTT during 3rd trimester and labor is associated with a very high chances of PROM and preeclampsia.

KEYWORDS: Hypercoagulable state, pregnancy, prothrombin time, activated partial thromboplastin time.**INTRODUCTION**

The coagulation system undergoes significant changes during pregnancy; increase in levels of clotting factors, decreased concentrations of some of the natural anticoagulants and diminishing fibrinolytic activity, thus producing a state of hypercoagulability. This phenomenon, supposedly due to hormonal changes, helps in maintaining placental function during pregnancy, protects from fatal hemorrhage during delivery but at the same time predisposes to thromboembolism, both during pregnancy and puerperium.^[1] There seems to be a state of low grade disseminated intravascular coagulation (DIC), which is most prominent during term and immediate post-partum period.^[2]

Activated partial thromboplastin time (aPTT) is generally used to assess coagulation disorders in patients

with abnormal bleeding due to deficiencies within the intrinsic coagulation cascade, for monitoring anticoagulant therapy with unfractionated heparin and for detecting inhibitors of blood coagulation which tend to produce prolonged aPTT.^[3] On the other hand, shortened aPTT has long been thought of as an artifact secondary to problematic blood collections, storage or processing leading to in-vitro activation. However, recent evidence suggests that shortened aPTT might actually reflect in-vivo events that might be associated with hypercoagulability.^[4] Use of different commercial reagents was also one of the controversies for a shortened aPTT but they have also been found to have a good agreement.^[5] Various pathological conditions have been found to present with a shortened aPTT and it has also been shown to be associated with significantly increased risk of thrombotic disorders and mortality.^[6] Recent studies established that shortened aPTT

independently predict first episodes and also subsequent recurrence of venous thromboembolism (VTE).^[7] The etiology of shortened aPTT related-thrombosis is unclear. High levels of plasma coagulation factors resulting in a pro coagulant misbalance may explain the increased tendency to thrombosis. Shortened aPTT is inversely related to plasma levels of coagulation factor VIII (FVIII) and thrombin-antithrombin (TAT) complex. Studies have found that the levels of most aPTT associated clotting factors were elevated in shortened aPTT test samples (i.e., FV, FVIII, FIX, FXI, FXII). Moreover, vWF levels and activity as well as pro coagulant phospholipid are also elevated in cases presenting with shortened aPTT.^[3,5]

Previous studies have documented a shortened aPTT levels during pregnancy [8, 9]. The finding of shortened aPTT in pregnant women can in part be explained by increase in levels of FV, FVIII, FIX and FXII [9]. Few researchers have also tried to formulate normative values of coagulation parameters according to the period of gestation.^[10-12] But it is also acknowledged that these values are to be interpreted in the light of the ethnicity, race and socio-economic background.^[10]

The present study is carried out to find the prevalence of shortened Prothrombin time (PT) and activated Partial thromboplastin time (aPTT) in pregnant women and also to find any possible correlation of an isolated shortened aPTT during 3rd trimester of pregnancy or labor with preeclampsia and PROM (Premature rupture of membranes).

MATERIALS AND METHODS

It was a retrospective study, including pregnant women, being followed up in the antenatal clinic of the Department of Gynecology and Obstetrics, Lady Hardinge Medical College, New Delhi. The study was conducted in the Department of Pathology, Lady Hardinge Medical College, New Delhi. Case records of all the pregnant women, newly registered in the antenatal clinic of our institute during a period of 1 month from July to August 2015 were reviewed and were included in the study after applying exclusion criteria. The inclusion criteria included: age > 18 years, available data of PT,

aPTT and subsequent follow up regarding PROM and preeclampsia. The exclusion criteria were: bad obstetric history/ recurrent miscarriages, antenatal hemorrhage during present or past pregnancy, personal or family history of known bleeding diathesis or history of taking anticoagulants. The women were followed both clinically and with relevant investigations, including PT and aPTT, performed during different trimesters as per the protocol of our institute. A total of 173 eligible women were included in the study. PT and aPTT was assessed using the ACL Elite Pro coagulation analyzer as per the manufacturer's guidelines. The controls for PT and for aPTT were taken as 11.0 and 29.0 seconds respectively. Shortened PT was taken as results less than 9.5 seconds and aPTT as 25.5 seconds [10, 11]. Correlation with clinical outcomes (PROM and preeclampsia) was done in cases with isolated shortened aPTT detected during 3rd trimester or labor. Data were collected on a pre-designed structured performa and managed on Microsoft Excel spreadsheet.

RESULTS

Out of 244 pregnant women newly registered during the study period, a total of 173 were included. One hundred and twenty four (71.7%) of enrolled pregnant women were found to have a shortened PT, aPTT or both. Among the women with a shortened coagulation profile, the most common abnormality was an isolated shortened aPTT (65/124) (Table 1).

Table: 1 PT and aPTT of pregnant women (n=173)

	PT and aPTT	Number (%)
1.	Normal or increased	49 (28.3%)
2.	Shortened PT	39 (22.5%)
3.	Shortened aPTT	65 (37.6%)
4.	Both (PT and aPTT) shortened	20 (11.6%)

Only 10 patients were in their 1st or 2nd trimester of pregnancy and 11 were tested at the time of labor, while majority were in 3rd trimester (83%). Table 2 summarizes the frequency of shortened PT and aPTT according to the time of pregnancy.

Table: 2 PT and aPTT according to pregnancy stage (n=124)

	Pregnancy stages	Shortened PT	Shortened aPTT	Both PT and aPTT shortened	Total
1.	1-2 trimester	04 (10%)	04 (6%)	02 (10%)	10 (8%)
2.	3 rd trimester	31 (80%)	56 (86%)	16 (80%)	103 (83%)
3.	Labour	04 (10%)	05 (8%)	02 (10%)	11 (8.9%)
4.	Total	39 (32%)	65 (53%)	20 (15%)	124

Among women with an isolated shortened aPTT detected during 3rd trimester or labor (n=61), 37 were found to

have premature rupture of membranes and 17 were diagnosed with preeclampsia (Table 3).

Table: 3 Association of shortened aPTT with preeclampsia and PROM in 3rd trimester/ labour

	Outcome	Number (%)
1.	Pre-eclampsia	17 (29.7 %)
2.	PROM	37 (60.6%)
3.	Uneventful	07 (11.5%)
4.	Total	61 (100%)

DISCUSSION

In this retrospective study, the authors looked into the PT and aPTT levels of 173 pregnant women during different trimesters of pregnancy and labor and also outcome of those with a shortened aPTT. The present study discloses a high prevalence of shortened PT (22.5%) and aPTT (37.6%); further, a shortened aPTT at 3rd trimester and labor was associated with a very high rate of PROM (60.6%) and preeclampsia (29.7%).

During pregnancy the concentrations of coagulation factors V, VII, VIII, IX, X, XII and von Willebrand factor rise significantly, accompanied by a pronounced increase in the concentration of plasma fibrinogen.^[11] Oestradiol induced alteration of triglyceride is probably responsible for these changes in coagulation and fibrinolysis.^[13] The very high rate of shortened coagulation parameters revealed by the present study is well in consistence with similar studies from other parts of the developing world.^[8]

Thrombophilia predisposes a woman for an increased risk of developing both early and late complications in pregnancy. These include recurrent miscarriages, PROM and late placental vascular-mediated problems (fetal loss, preeclampsia, placental abruption and intra-uterine growth restriction).^[14] The risk of VTE increases by 4-5 times during pregnancy and 20-100 fold during immediate post-partum period. The incidence of VTE during pregnancy ranges between 0.49-1.72 per 1000 deliveries; accounting for 1.1 deaths per 100,000 deliveries and about 10% of all maternal deaths.^[15]

A shortened aPTT was associated with very high incidence of PROM and preeclampsia in the present study. Hypercoagulable state has been linked to PROM in previous studies as well^[16], and the same is reflected in the present series. A shortened aPTT is also seen in women with preterm delivery; this could be due to the slightly elevated levels of vWF antigen and factor VIII activity.^[17] Han et al^[18], on the other hand had demonstrated an increased aPTT in pregnant women with preeclampsia, a finding contrary to our study.

Some limitations were noted and must be acknowledged in this study. It was a cross-sectional study with PT and aPTT measured only once; and other parameters of coagulation and fibrinolytic pathway were not measured; there was no age matched non pregnant control group; Despite these limitations, assuming that the sample of patients studied is representative; the present results indicate a high prevalence of shortened PT and aPTT and associated risk of preeclampsia and PROM in pregnancy

in the given setting. Careful monitoring of patients with shortened aPTT is expected to reduce associated morbidity and mortality and at the same time allows risk stratification of these patients

CONCLUSION

The present study shows a very high prevalence of shortened PT and aPTT during 3rd trimester of pregnancy and labor when chances of bleeding are highest, also a relation between shortened aPTT during this time with PROM and preeclampsia. Further studies with larger cohorts and other coagulation parameters are required to predict clinical outcomes in pregnant women with shortened coagulation profile.

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